

REMARKS

Claims 1-21, 24-27 and 50-66 are pending. New claim 85 is added and claims 17-20, 24-27 and 50-66 are cancelled in the present response. Claims 22-23, 28-49 and 67-84 have been withdrawn in a previous response due to the Examiner's restriction requirement. These claims have been cancelled or withdrawn from consideration without prejudice to, or disclaimer of, the subject matter thereof. Applicant reserves the right to file divisional and continuing applications directed to the subject matter of any claim cancelled or withdrawn for any reason.

The present amendments to the claims place the application in better condition for examination. It is submitted that no new matter has been introduced by the present amendments, and entry of the same is respectfully requested. By these amendments, Applicant does not acquiesce to the propriety of any of the Examiner's prior rejections and does not disclaim any subject matter to which Applicant is entitled. *Cf. Warner Jenkinson Co. v. Hilton-Davis Chem. Co.*, 41 USPQ.2d 1865 (US 1997).

I. Provisional Non-Statutory Double Patenting Rejections

The Examiner provisionally rejected claims 1-21, 24-27 and 50-66 on the ground of nonstatutory obviousness-type double patenting over claims 1, 10 and 34-53 of copending Application No. 11/003,006 (the '006 application) in view of Campbell (Cloning & Stem Cells, 3(4): 201-208 (2001)). Office Action mailed August 15, 2006 ("OA"), page 3. Applicant respectfully traverses this rejection.

As required by the Manual of Patent Examining Procedure ("MPEP"), § 804-II-B-1,

[i]n determining whether a nonstatutory basis exists for a double patenting rejection, the first question to be asked is – does any claim in the application define an invention that is merely an obvious variation of an invention *claimed in the patent?* ... Obviousness-type double patenting requires rejection of an application claim when the claimed subject matter is **not patentably distinct** from the subject matter claimed *in a commonly owned patent* ...

(**bolded** emphasis in original; *italicized* emphasis added). Applicant does not agree with the propriety of asserting a double patenting rejection in view of the '006 application and a non-related and non-commonly owned reference that is not a patent application. Indeed the quoted MPEP section provides no basis for a non-

statutory obviousness type double patenting rejection that is based on anything other than a commonly owned patent.

Even if the Examiner's reliance on a non-related and non-commonly owned reference in combination with the '006 application was proper, the Examiner has nonetheless failed to establish a *prima facie* case of obviousness. In order to establish a *prima facie* case of obviousness, the Examiner must show that three basic criteria have been met: (1) that there is a suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference into the claimed invention; (2) that there is a reasonable expectation of success based on the combination; and (3) that the prior art reference teaches or suggests all of the claim limitations of the present application. MPEP § 706.02(j). Applicant submits that the Examiner has not established a *prima facie* case of obviousness for rejecting claims 1-21, 24-27 and 50-66 on the ground of nonstatutory obviousness-type double patenting over claims 1, 10 and 34-53 of the copending '006 application in view of Campbell (Cloning & Stem Cells, 3(4): 201-208 (2001)).

First, the Examiner stated, in part, "given the instant claims in view of Campbell, it would have been obvious for one of skill in the art to use an extrusion-enucleated oocyte in the methods of the '006 claims." OA, page 4. Because the Examiner has provided no support for this statement, however, Applicant respectfully disagrees. "Obviousness cannot be established by combining the teaching of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 221 USPQ 929, 932, 933 (Fed. Cir. 1984). There is no support for the combination here, and the Examiner has done nothing more than make the above-noted assertion. Accordingly, there is no suggestion or motivation to combine either in the references themselves or in the knowledge generally available to one of ordinary skill in the art and the first required criterion to establish *prima facie* obviousness has not been met.

Regarding the second criterion required to establish *prima facie* obviousness, the Examiner failed to show or to state that the relied-upon combination of references would provide a reasonable expectation of success. Applicant finds this lack of showing noteworthy in light of the Examiner's long discussion of the "uncertainty" inherent in the present field to support the later described 35 U.S.C. §

112 ¶ 1 rejections. Accordingly, the Examiner has provided no evidence of a reasonable expectation of success, and, as a result, the second required criterion of *prima facie* obviousness also has not been met.

Finally, and in regard to the third criterion of obviousness, the combined references do not teach or suggest all of the claim limitations of the claims as originally pending or as presently amended. The '006 application does not disclose the use of a generically enucleated egg. Without this disclosure, the '006 application does not teach or suggest all of the claim limitations of the present application. Thus, and for all the reasons stated above, the Applicant respectfully requests that the Examiner reconsider and withdraw the provisional nonstatutory obviousness-type double patenting rejections of claims 1-21, 24-27 and 50-66.

II. Claim Rejections Under 35 U.S.C. § 101

The Examiner next rejected claims 24-27 under 35 U.S.C. § 101 as directed to non-statutory subject matter. OA at 4. Applicant respectfully traverses. The Examiner asserted that these claims cover human beings and animals produced by nuclear transfer that would not otherwise be distinguishable from naturally-occurring animals. *Id.* While the Applicant does not agree with the propriety of these rejections, Applicant has nonetheless cancelled claims 24-27 in the present response. Therefore, this rejection is moot and Applicant respectfully requests reconsideration and withdrawal of the same. Applicant also reserves the right to file continuing applications directed to this cancelled subject matter.

III. Claim Rejections Under 35 U.S.C. § 112

Claims 1-21, 24-27 and 50-66 were rejected under 35 U.S.C. § 112, ¶ 1 as failing to comply with the enablement requirement. The Applicant respectfully traverses.

The Examiner based the present 35 U.S.C. § 112, ¶ 1 rejections on the Examiner's application of the *In re Wands* factors (*In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988); MPEP § 2164.01(a)) to the present invention. The Examiner's enablement rejections are improper, however, due to an incomplete analysis under *In re Wands* ("It is improper to conclude that a disclosure is not enabling ... while ignoring one or more of the [factors]. The Examiner's analysis must consider all evidence related to each of these factors, and any conclusion of nonenablement must be based on the evidence as a whole." MPEP § 2164.01(a) quoting *In re Wands*, 858 F.2d at 737, 740). Here, the Examiner did not analyze the *In re Wands*

factor of: the level of one of ordinary skill in the art. Because the level of ordinary skill in the art of the claimed invention is exceedingly high, this factor would weigh in favor of enablement and therefore, the entirety of the Examiner's analysis is flawed. Because the Applicant has nonetheless amended the claims in an effort to facilitate prosecution of the present application, the Applicant requests that the Examiner revisit the enablement issue in light of all the *In re Wands* factors, the present claim amendments and the Applicant's explanations concerning the *In re Wands* factors provided below.

A. Nature of the Invention

In the August 15, 2006 Office Action, the Examiner stated that the nature of the claimed invention is directed to "methods of introducing nuclei along with one or more molecular components into an egg; culturing the egg to produce a viable embryo; transferring the embryo to the oviducts of a female; and producing a cloned animal." *Id.* at 5. The claims as amended, however, are directed to introducing a nucleus along with one or more molecular components (selected from the group consisting of a centrosome protein, a centrosomal component from a sperm centrosome, a mitotic motor protein, and combinations thereof) into an enucleated egg; activating the egg; and culturing the egg to produce a viable primate embryo. Thus, the Examiner's previous position regarding the claims does not reflect the correct nature of the invention as defined by the presently pending claims. As such, the Examiner's previous analysis no longer applies and a re-evaluation is required.

B. Breadth of the Claims

The Examiner stated that the claims read on "methods of introducing donor nuclei into recipient eggs by methods other than SCNT, using a donor nuclei and recipient egg of the same or different species of animal, using any type of donor nuclei and any type of recipient egg to produce any cloned animal." *Id.* at 5-6. If the Examiner considered this breadth too broad in light of the specification, the Examiner was required to identify the subject matter that was considered to be enabled. MPEP 2164.08. The Examiner did not do this. Further, the Applicant reminds the Examiner that "the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims." MPEP § 2164.08 quoting *In re Fisher*, 427 F.2d 833, 839 (CCPA 1970). Therefore, and for all the reasons stated above, any rejection based in part on this factor was improper and must be reconsidered.

When reconsidering this *In re Wands* factor the Examiner should note that the claims as presently amended are directed to introducing a nucleus along with one or more molecular components (selected from the group consisting of a centrosome protein, a centrosomal component from a sperm centrosome, a mitotic motor protein, and combinations thereof) into an enucleated egg; activating the egg; and culturing the egg to produce a viable primate embryo. The present amendments to the claims create a more direct correlation between the guidance provided in the specification and the invention as now claimed and Applicant asserts that this breadth is fully enabled under 35 U.S.C. § 112 ¶ 1.

C. Guidance of the Specification/The Existence of Working Examples

The Examiner states that the specification teaches that one limitation associated with SCNT in primates is that removal of the donor egg DNA, along with spindle and spindle proteins, can cause problems associated with later growth of the egg. The Examiner also states that the “specification provides no guidance with regard to any implantation or pregnancies that resulted from NT constructs transferred to surrogate mothers.” *Id.* at 6. The Examiner also states that the specification teaches that previously there had been no evaluation of the centrosomes or structural/molecular motor proteins role in bipolar spindle assembly after NT and that dysfunctional centrosomes, as well as missing NuMA and HSET kinesin result in mitotic multiple spindles with misaligned chromosomes. *Id.* Of particular relevance to the Examiner’s application of this *Wands* factor, the amended claims are drawn to the production of primate embryos, a process that is thoroughly described in the specification and in light of the knowledge of one of ordinary skill in the art (see, for example and without limitation, paragraphs 49, 50, 52 and 59-65 of the present application). Further, the presently pending claims are directed to adding specific molecular components that have been found deficient in enucleated eggs. Supporting the guidance and teachings found in the present specification, post filing art has concluded that “[t]he NuMA turbulence associated with disordered chromosome organization that was found in some SCNT-produced embryos in this study was consistent with development failure.” Zhou *et al.*, A Comparative Approach to Somatic Cell Nuclear Transfer in the Rhesus Monkey, Human Reproduction, 21(10), 2564-2571 (2006). Based on the foregoing, this factor supports the relevant guidance provided in the specification and thus this factor weights in favor of 35 U.S.C. § 112 ¶ 1 enablement.

D. State of the Art/Predictability of the Art

The Examiner begins this section of the analysis with a statement that the claims are drawn to the cloning of any animal. *Id.* at 7. However, the presently pending claims are directed to the production of primate embryos as embryos are defined within the specification. Thus, the Examiner's analysis regarding this factor does not correlate with the presently pending claims.

In this portion of the analysis, the Examiner cites a number of publications. For example, the Examiner cites Oback (Cloning & Stem Cells, 4(2): 147-168 (2002)) for the proposition that of more than 200 distinct cell types that have been tested as nuclear donors, many repeatedly fail to generate viable offspring. *Id.* The Examiner admits, however, that all support the development of blastocysts. *Id.* The Examiner next cites Oback for statements made by both Wakayama and Yanagimachi and Kato supporting the position that the production of live offspring following SCNT is uncertain. *Id.* Again, however, the present claims are drawn to the production of primate embryos so these references are not relevant to the presently claimed invention.

The Examiner's discussion of the predictability of SCNT then continues to focus on the unpredictability of producing live cloned animals with the process. For example, the Examiner quotes Li *et al.* (Reprod. Bio. & Endocrin., 1(84):1-6 (2003)) for the proposition that "if it would be routine experimentation to produce cloned animals, then one could expect that any donor cell could be successfully used to produce any species of animal." *Id.* at 9. Likewise, the Examiner cites the Li article for the proposition that, "[m]ost cloned embryos lose their development abilities during pre-implantation and gastrulation. Moreover, the surviving adults often show abnormalities." *Id.* The Examiner next cites McEvoy *et al.* (Reprod. Supp., 61: 167-182 (2003)) for the proposition that "NT-derived ruminants is an inefficient process that generally fails to generate viable offspring." *Id.* Likewise, the Ng reference cited by the Examiner relates to the production of live primate offspring through SCNT methods ("ninety-three reconstructed embryos were transferred into 31 recipients, which results in 7 pregnancies, but no live births"). *Id.* at 10. As stated, however, the claims of the present invention are drawn to the production of primate embryos. Therefore, none of these references are relevant to the enablement of the presently claimed invention. As such, these references as applied to this *In re Wands* factor do not support a 35 U.S.C. § 112, ¶ 1 rejection.

Regarding the Ng reference specifically, the Examiner cites this reference for the proposition that "NT embryos were capable of spindle formation." Specifically, the Examiner alleges that this paper reports that 14.8% of somatic cell chromosomes will condense into normal PCC spindle within about two hours of injection." *Id.* at 11. Based on this result, the Examiner concludes that NT-non human primates are capable of spindle formation. *Id.* at 12. However, this paper confirms that 85.2% of somatic cell chromosomes *do not* condense into normal PCC spindles within about two hours of injection, and importantly, the Examiner provides no evidence that the authors of this reference evaluated any cells for the presence or absence of appropriate levels of molecular components as contemplated by the presently claimed invention. Therefore, this reference also has little bearing on the presently claimed invention. As such, and based on the proceeding discussion, this factor also does not support a 35 U.S.C. § 112, ¶ 1 rejection.

E. The Amount of Experimentation Necessary

The Examiner states that although the art teaches specific SCNT has been successful in specific species using specific cells, the genus of cloning animals by SCNT fails to be enabled by these discrete embodiments. *Id.* at 13. The Examiner goes on to argue that the state of the art shows that undue experimentation would be necessary in order to determine what parameters would be required in order to arrive at producing a live-born, cloned animal as broadly claimed. *Id.* The claims as pending, however, are directed to the production of primate embryos. Importantly, primate somatic cell nuclear transfer "produces cloned embryos routinely and reliably." Simerly *et al.*, Embryogenesis and Blastocyst Development After Somatic Cell Nuclear Transfer in Nonhuman Primates: Overcoming Defects Caused by Meiotic Spindle Extraction, *Developmental Biology*, 276, 237-252 (2004). Thus, the Examiner's application of this factor is not relevant to the pending claims. Further, because the production of SCNT primate embryos is "routine and reliable" according to those of ordinary skill in the art, this factor favors enablement under 35 U.S.C. § 112, ¶ 1. Even if the production of primate embryos were not routine and reliable in some instances, however, those of ordinary skill in the art would recognize that experimentation could be required before successfully practicing the described invention. This anticipated experimentation is inherent in the highly specialized field of somatic cell nuclear transfer and should not be used as an argument against enablement.

F. The Level of One of Ordinary Skill in the Art

In the previous enablement analysis, the Examiner failed to specifically address the *In re Wands* factor of the level of one of ordinary skill in the art. As such, this analysis was improper, incomplete and must be revisited. Importantly, in the field of somatic cell nuclear transfer, the level of one of ordinary skill in the art is exceedingly high. This is a specialized and technical field requiring years of training to enter. Thus, those of ordinary skill in the art can be expected to have a high degree of knowledge regarding the techniques and considerations to be used and taken when performing experiments relating to the teachings of the present application and this factor weighs in favor of enablement.

In *In re Wands*, Federal Circuit held that the specification at issue was enabling because: “‘there was considerable direction and guidance’ in the specification; there was ‘a high level of skill in the art at the time the application was filed;’ and ‘all of the methods needed to practice the invention were well known.’” MPEP § 2164.01(a) quoting *In re Wands*, 858 F.2d at 737, 740. The preceding discussion shows that the presently pending claims are also fully enabled under an *In re Wands* analysis. Specifically, the nature of the invention and the breadth of the claims relate to introducing a nucleus along with one or more molecular components (selected from the group consisting of a centrosome protein, a centrosomal component from a sperm centrosome, a mitotic motor protein, and combinations thereof) into an enucleated egg; activating the egg; and culturing the egg to produce a viable primate embryo. This breadth of the claims is directly commensurate with the teachings provided by the present application’s specification (see, for example and without limitation, paragraphs 49, 50, 52 and 59-65 of the present application). Regarding the state and predictability of the art and the amount of experimentation necessary, the production of primate embryos using SCNT is “routine and reliable” according to those of ordinary skill in the art. Further, the sophisticated nature of the field and the level of ordinary skill of those who practice within it is exceedingly high. Therefore, all of these factors support enablement under an *In re Wands* analysis and 35 U.S.C. § 112 ¶ 1. As such, the Applicant respectfully requests that the present 35 U.S.C. § 112 ¶ 1 rejections of claims 1-21, 24-27 and 50-66 be reconsidered and withdrawn.

IV. Claim Rejections Under 35 U.S.C. § 102

The Examiner made a number of claim rejections under 35 U.S.C. § 102. Applicant asserts that based on the Examiner's overly broad interpretation of "molecular components" (see, OA, page 14), none of these rejections were proper. Based on the present claim amendments, however, the references relied on in the Examiner's 35 U.S.C. § 102 rejections are even *further* distinguished from the present claims. Thus, while the following rejections are addressed in light of how the claims presently are presented, one should understand that patentable distinctions existed before these amendments occurred and as a result, they should not be read to limit the scope of the claims.

The Examiner first rejected claims 1-5, 21, 24, 50-54 and 66 under 35 U.S.C. § 102(b) as anticipated by Schnieke *et al.* (Science, 278: 2130-2133, 19 December 1997). *Id.* at 14. Applicant respectfully traverses. According to the Examiner, Schnieke teaches the production of sheep embryos by nuclear transfer wherein the fibroblast donor cells were co-transfected with a neomycin resistance marker and the human coagulation factor IX genomic construct. *Id.* The present application is directed to the production of primate embryos through nuclear transfer and that element of the claims is not taught or enabled by Schnieke. Therefore, Applicant respectfully requests that these claim rejections be reconsidered and withdrawn.

Next, the Examiner rejected claims 1-5, 7, 21, 24, 50-54, 56 and 66 under 35 U.S.C. § 102(b) as anticipated by Stelchenko *et al.* (U.S. Pat. No. 6,011,197). *Id.* at 15. Applicant respectfully traverses. According to the Examiner, Stelchenko teaches the production of bovine NT embryos using totipotent cells as donor cells and enucleated bovine oocytes as recipient cells and the production of liveborn calves from the embryos. *Id.* The present application, however, is directed to the production of primate embryos through nuclear transfer and that element of the claims is not taught or enabled by Stelchenko. Therefore, Applicant respectfully requests that these claim rejections be reconsidered and withdrawn.

The Examiner next rejected claims 1-5, 7, 13, 21, 24, 50-54, 62 and 66 under 35 U.S.C. § 102(a) or alternatively under 35 U.S.C. § 102(e) as anticipated by Collas *et al.* (U.S. Pub. No. 2003/0046722). *Id.* at 16. Applicant respectfully traverses. According to the Examiner, Collas teaches methods of nuclear transfer that include contacting the donor nucleus with one or more conditions that allow for the formation

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of a chromatin mass; subsequent rounds of nuclear transfer of the resultant NT unit; and that the donor cell can be permeabilized by incubation in a reprogramming media containing a mitotic extract that contains nuclear or cytoplasmic components that can add a factor to the nucleus. *Id.* This reference, however, does not teach or enable the element of the addition of molecular components as presently defined in the claims into an enucleated egg to produce a primate embryo and therefore does not anticipate the claims under 35 U.S.C. §§ 102(a) or (e). As such, Applicant respectfully requests that these claim rejections be reconsidered and withdrawn.

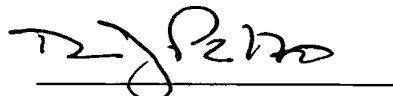
The Examiner next rejected claims 24, 25 and 27 under 35 U.S.C. § 102(b) as anticipated by Vanderzwalmen *et al.* (Hum. Reprod., 7(4): 537-544 (1992)) and claims 24-26 under 35 U.S.C. § 102(b) as anticipated by Thomson (U.S. Pat. No. 5,843,780). *Id.* at 16-17. Applicant respectfully traverses. Nonetheless, these rejections are moot based on Applicant's present cancellation of claims 24, 25 and 27. Therefore, Applicant respectfully requests reconsideration and withdrawal of the same.

CONCLUSION

Applicant has properly and fully addressed each of the Examiner's grounds for rejection. Applicant submits that the present application is now in condition for allowance. If the Examiner has any questions or believes further discussion will aid examination and advance prosecution of the application, a telephone call to the undersigned is invited.

If there are any further fees due in connection with the filing of the present reply, please charge the fees to undersigned's Deposit Account No. 50-1067. If a fee is required for an extension of time not accounted for, such an extension is requested and the fee should be charged to undersigned's deposit account.

Respectfully submitted,



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